



King's Research Portal

DOI:

[10.1016/j.canep.2018.09.001](https://doi.org/10.1016/j.canep.2018.09.001)

Document Version

Peer reviewed version

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Tataru, D., Spencer, K., Bates, A., Wieczorek, A., Jack, R. H., Peake, M. D., Lind, M. J., & Lüchtenborg, M. (2018). Variation in geographical treatment intensity affects survival of non-small cell lung cancer patients in England. *Cancer Epidemiology*, 57, 13-23. <https://doi.org/10.1016/j.canep.2018.09.001>

Citing this paper

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

General rights

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

Highlights

- In England, the access to curative treatment varied by geographical area
- Living far from a treatment centre reduces the likelihood of surgical treatment
- The most deprived patients with greatest travel time were least likely to have surgery
- Increasing curative treatment rates were associated with lower population mortality

Variation in geographical treatment intensity affects survival of non-small cell lung cancer patients in England

Daniela Tataru^{*a}, Katie Spencer^{*b}, Andrew Bates^c, Andrzej Wiecezorek^d, Ruth H Jack^a, Michael D Peake^{a,e,f}, Michael J Lind^{d,g}, Margreet Lüchtenborg^{a,h}

^a National Cancer Registration and Analysis Service, Public Health England, Wellington House, London, UK

^b Faculty of Medicine and Health, Leeds Institute of Cancer & Pathology, University of Leeds

^c University Hospital Southampton NHS Foundation Trust, Southampton, UK;

^d Hull and East Yorkshire NHS Trust, Hull, UK

^e Institute for Lung Health, University of Leicester, Leicester, UK

^f Centre for Cancer Outcomes, University College London Hospitals, London, UK

^g Hull York Medical School, University of Hull, UK

^h Department of Cancer Epidemiology, Population and Global Health, Division of Cancer Studies, Faculty of Life Sciences & Medicine, King's College London, London, UK

*These authors contributed equally to this work

Correspondence to:

Dr Daniela Tataru

National Cancer Registration and Analysis Service

Public Health England

Wellington House

133-155 Waterloo Road

London SE1 8UG

Tel: 020 3682 0803

Email: daniela.tataru@phe.gov.uk

Word count: abstract 250; manuscript 4767; highlights 47;

Abstract

Objectives. We aimed to determine the geographical variation in the proportion of non-small cell lung cancer (NSCLC) patients undergoing curative treatment and assess the relationship between treatment access rates and survival outcomes.

Methods. We extracted cancer registration data on 144,357 lung cancer (excluding small cell tumours) patients diagnosed between 2009 and 2013. Surgical and radiotherapy treatment intensity quintiles were based on patients' Clinical Commissioning Group (CCG) of residence. We used logistic regression to assess the effect of travel time and case-mix on treatment use and Cox regression to analyse survival in relation to treatment intensity.

Results. There was wide variation in the use of curative treatment across CCGs, with the proportion undergoing surgery ranging from 8.9% to 20.2%, and 0.4% to 16.4% for radical radiotherapy. The odds of undergoing surgery decreased with socioeconomic deprivation (OR 0.91, 95% CI 0.85-0.97), whereas the opposite was observed for radiotherapy (OR 1.16, 95% CI 1.08-1.25). There was an overall effect of travel time to thoracic surgery centre on the odds of undergoing surgery (OR 0.81, 95% CI 0.76-0.87 for travel time >55 min vs ≤15 min) which was amplified by the effect of deprivation. No clear association was observed for radiotherapy. Higher mortality rates were observed for the lower resection and radiotherapy quintiles (HR 1.08, 95% CI 1.04-1.12 and HR 1.06, 95% CI 1.02-1.10 for lowest vs. highest resection and radiotherapy quintile).

Conclusion. There was wide geographical variation in the use of curative treatment and a higher frequency of treatment was associated with better survival.

Keywords: non-small cell lung cancer; curative treatment; surgical resection; radical radiotherapy; geographical variation; England

1 Introduction

Lung cancer is one of the three most common cancers in England with 36,637 newly diagnosed cases in 2015 [ONS, 2017]. It is also the commonest cause of death from cancer with 30,520 deaths annually, representing 21% of all cancer deaths [ONS, 2017]. Although survival rates for lung cancer have been improving in England in recent years [1], they remain poor compared with many other cancers. In addition, survival rates in England are worse than those reported from a number of other countries with equivalent expenditure on healthcare [2, 3].

Almost 90% of all lung cancers diagnosed in England have non-small cell histology or are diagnosed on clinical grounds without tissue confirmation [4]. Fit, early stage non-small cell lung cancer (NSCLC) patients can be offered potentially curative treatment, either with surgical resection or radiotherapy, often combined with adjuvant chemotherapy. Wide variation in usage of surgical resection for NSCLC patients across England and a clear association between resection rate and survival has previously been demonstrated [5]. Such variation has also been demonstrated in other European countries [6, 7]. This may in part be attributable to patient and disease-related factors with performance status, comorbidity, age (with associated increasing frailty and patient choice) and disease stage all justifiably impacting upon the clinical decision-making process [8-10]. Differing interpretation of the clinical evidence supporting cancer treatment decisions may, however, result in varying practice [11] and previous small-scale studies have demonstrated wide variation in Multi-Disciplinary Team (MDT) recommendations for identical presentations [12]. As such, variation in quality and access to stage specific treatments may, in part, underpin the relatively poor outcomes seen for NSCLC in the UK [3]. Analyses which focus upon surgery alone will, however, have a limited scope in a population often unfit for such an approach. In this often co-morbid population of NSCLC patients, radical radiotherapy is frequently more appropriate. Moreover, where surgical resection is not possible, radical radiotherapy can offer potential cure. As such, in order to assess effectiveness of curative treatment for NSCLC at the population level both treatment modalities should be considered. A priori, one could hypothesize that CCGs with high surgical resection rates would have low radical radiotherapy rates and vice versa, due to case-mix factors or historical local treatment preferences favouring one treatment over the other. Alternatively, one could hypothesize that CCGs that had high surgical resection rates also had high radical radiotherapy rates owing to a general appetite for curative treatment.

This study aimed to determine the proportion of NSCLC patients in England undergoing potentially curative treatment and its geographical variation. We aimed to assess the impact of patient and tumour characteristics, and distance to nearest treatment centre on treatment rates and determine the relationship between rates of access to curative treatment and population level survival outcomes.

2 Methods

2.1 Study population

Data on 168,634 lung cancers (International Classification of Diseases [version 10] (ICD10) codes C33 to C34) diagnosed in England between 1 April 2009 and 31 December 2013 were extracted from the National Cancer Registration Dataset [AV2013], held by the National Cancer Registration and Analysis Service at Public Health England. We excluded 18,492 cancers with small cell histology (ICD-O-2 classification morphology codes 8041-8045), 3,865 cancers identified from death certificates only (DCO), and 113 cases without a recorded National Health Service (NHS) number. Only the first lung cancer recorded for each patient was included, which affected 1,689 patients with multiple primary lung cancers. The analyses focussed on adult lung cancer patients only, and excluded 43 patients under the age of 15 and over 100. Finally, we excluded 75 patients with unknown vital status. The final data set thus included 144,357 adult NSCLC patients, of whom 68% had a histological and/or cytological confirmation.

2.2 Patient and tumour characteristics

Information on patient demographics and tumour characteristics (including stage, anatomical topography and morphology) were extracted from the core cancer registration data. Information on death was obtained from the Office for National Statistics (ONS).

Socioeconomic deprivation (SED) is based on the income domain of the Indices of Deprivation (version 2015) [13]. Lower Super Output Areas (LSOAs, geographic areas of a consistent size that cover a population of approximately 1,500 persons) were grouped into five SED quintiles, each containing 20% of the population of England. The least deprived quintile was labelled 1 and the most deprived 5.

Patients were assigned to an SED quintile based on their postcode of residence at the time of diagnosis.

Performance status at diagnosis was available through patient level linkage with the National Lung Cancer Audit data [14].

Comorbidity information was obtained from linked in-patient Hospital Episode Statistics (HES 2015) records [15]. Diagnoses (excluding cancer, for which information was retrieved from cancer registration records) from hospital admissions 27 months to 3 months prior to the lung cancer diagnosis were used to calculate the weighted Charlson comorbidity scores (CCS) [16]. The resulting scores were grouped into four categories of increasing severity (CCS 0, 1, 2, 3+). A small proportion of patients (0.9%) did not have a linked HES record and were assumed to have a CCS of 0.

2.3 Treatment

Information on surgical resection was retrieved from linked in-patient and day-case HES records. The cancer registration records were linked to HES records using a matching algorithm based on patient's NHS number, date of birth, sex and postcode at diagnosis. Less than 1% of records did not have a linked inpatient HES record and for these patients we assumed that they did not have any comorbid conditions. Surgical procedures recorded in the HES dataset are coded using the Office of Population,

Censuses and Surveys Classification of Surgical Operations and Procedures (4th revision, OPCS-4) [17]. Types of surgical resections were included as previously defined [18]: lobectomy or bilobectomy (68%), partial lobectomy or wedge resection (16%), pneumonectomy (12%), sleeve resection (1%), and other less common procedures (other or unspecified excisions of (or lesions of) trachea, carina, lung, and chest wall, 4%). Surgical procedures from one month before to six months after the date of diagnosis were included. If patients had more than one recorded surgical procedure, the most extensive procedure was used in the analysis.

Information on radiotherapy treatments was retrieved from the linked summary records in the national Radiotherapy Dataset (RTDS). The RTDS contains information on all episodes of radiotherapy delivered, but does not consistently capture the treatment intent, whether it be radical, adjuvant or palliative. In addition, disease coding varies between centres, for example, total attendances are captured in some centres rather than intended fractionation patterns, and radiation dose is not always recorded. We considered all episodes starting within six months from date of diagnosis for which a treatment site code for lung cancer (ICD 10 C33-C34) or unspecified respiratory tract cancer (C78, C80, D38, D02) was recorded in the RTDS. When information on the total radiation dose used was missing, the radiotherapy treatment intent was derived using criteria based on clinical guidelines. Thus, radical treatment was defined as: patients with at least one radiotherapy treatment summary record with either 15 or more attendances (with or without recorded dose); 3, 5 or 8 attendances with a dose higher than 50Gy (stereotactic ablative radiotherapy, SABR); or 3, 5 or 8 attendances without a dose but with stage I or II (reflecting TNM stage I through IIA (N0)) treated at a radiotherapy centre known to have performed SABR during the study period. The identification of SABR treatment was validated within two treating centres. In addition, patients with two radiotherapy episodes delivered to the chest within 2 weeks of each other and which together summed up to more than 15 attendances were classified as having had radical radiotherapy treatment. Lung cancer patients without a linked RTDS record were deemed to have received no radiotherapy treatment. If a patient underwent surgical resection and adjuvant radiotherapy, this was considered as primary surgical treatment in the analyses.

To study geographical variation in treatment activity, we calculated the proportion of patients undergoing potentially curative treatment (surgical resection or radical radiotherapy) in each of the 211 Clinical Commissioning Groups (CCG). Because the two treatment modalities pertain to distinct groups of lung cancer patients, separate treatment intensity quintiles were created for surgical resection and radical radiotherapy, where Q1 is the quintile with the lowest and Q5 is the quintile with the highest treatment intensity. Patients were allocated to one of these quintiles based on their residential postcode at diagnosis linked to a CCG.

Travel time was calculated for all patients from their residential postcode at the time of diagnosis to their nearest treatment centre, using the ArcGIS Spatial Analyst module [19]. Given that thoracic surgical centres and radiotherapy treatment centres are not always co-located, distance to each of these was

assessed separately. Because the variation in travel time to nearest surgical treatment centre was greater than that to radiotherapy centre, we categorised them separately as 0-15, 16-25, 26-35, 36-55, >55 minutes for nearest thoracic surgical centre and 0-10, 11-20, 21-30, 31-40, >40 minutes for nearest radiotherapy treatment centre. We assumed that each patient was treated at the nearest facility and used the ArcGIS to calculate the shortest travel distance to it. It is recognised that in some cases this would not be the treating centre, however, identifying the geographical extent of each treating centre's catchment was not possible due to the lack of fixed health administrative boundaries, and thus nearest centre was used. Inaccurate or obsolete residential postcodes gave rise to missing travel times (0.5%).

2.4 Data analysis

The distribution of the patient characteristics (age, sex, SED, performance status, comorbidity) and tumour characteristics (stage, topography and morphology) were tabulated among all NSCLC patients and among patients undergoing surgical resection or radical radiotherapy. We used the Mantel-Haenszel test with 1 degree of freedom to assess the differences in case-mix by type of curative treatment, with the exception of age for which a Kruskal-Wallis rank test with 2 degrees of freedom was used.

The proportions of patients undergoing potentially curative treatment, radical radiotherapy and surgical resection by CCG were plotted. To assess the relationship between the two curative treatment modalities at CCG level, a scatterplot depicting the proportion of NSCLC patients undergoing either radical radiotherapy or surgical resection by CCG was created.

We used univariable and multivariable logistic regression to assess the association of distance to nearest treatment centre, patient and tumour characteristics with surgical resection and radical radiotherapy. We computed χ^2 values and p-values for trend and heterogeneity, where appropriate. To assess the combined effect of travel time and socioeconomic deprivation on the likelihood of receiving treatment the odds ratios for undergoing surgical resection or receiving radical radiotherapy were calculated relative to the least deprived quintile group living closest to a thoracic centre or a radiotherapy centre, respectively.

Cox proportional hazards regression analyses were used to assess the association between CCG treatment intensity quintiles of surgical resection and radical radiotherapy and survival. For patients not undergoing curative treatment survival time was calculated from the date of diagnosis to death or censoring date. In order to avoid immortal time bias, for patients undergoing treatment survival time was calculated from the date of surgery or the starting date of radical radiotherapy. All patients were followed up until the date of death or censored on 31/12/2016. Multivariable models included CCG treatment intensity (surgical resection or radical radiotherapy) quintile with adjustment for age, sex, SED, performance status, comorbidity and disease stage. In addition to standard Cox regression models, we ran shared-frailty Cox models with CCG as a random effect to account for potential unobserved variation in survival related to living in distinct geographical areas. We found a significant frailty effect for all

models considered and therefore the results from the shared-frailty Cox models are reported here. We computed χ^2 values and p-values for trend and heterogeneity, where appropriate.

To account for missing data, we also performed analyses based on imputed data. We used multiple imputation by chained equations to impute the missing data for stage and performance status. Twenty imputed datasets were created. We imputed the missing values for stage and performance status treatment using a model that included travel time, diagnosis year, age, sex, socio-economic deprivation, comorbidity, morphology, topography and survival time without interaction terms.

All statistical analyses were carried out using Stata version 13.1 (StataCorp, Texas, USA).

3 Results

Table 1 shows the patient and tumour characteristics of 144,357 NSCLC patients. The median age was 73 years (IQR 65-80), and the majority of patients were male (55.4%). Since we included patients from 1 April 2009 to the end of 2013, there were relatively fewer patients diagnosed in 2009 included in this study compared to the other years (15.2% in 2009, compared to 20.6, 21.1, 21.7, and 21.3% of patients diagnosed in 2010-2013). There was a clear gradient of NSCLC patients predominantly living in areas with higher socioeconomic deprivation (26.0% in the most deprived versus 14.0% in the least deprived socioeconomic deprivation quintile). Performance status was unknown for 31.7% of patients, 33.5% of patients did not have a stage recorded, 26.7% had an unspecified topography and 32.0% did not have a histological confirmation.

Of all NSCLC patients, 20.6% underwent potentially curative treatment: 14.0% underwent surgical resection and 6.6% underwent radical radiotherapy. The proportions of patients undergoing surgical resection increased from 12.2% in 2009 to 15.5% in 2013 and radical radiotherapy from 5.5% to 7.8% during the same period. Both surgical resection and radical radiotherapy offer potential cure to NSCLC patients, but patients undergoing either treatment modality differ. Whereas patients with stage I and II may be candidates for surgical resection, radical radiotherapy or chemoradiotherapy is usually the primary treatment modality for potentially curable stage III NSCLC. Patients who underwent surgical resection were younger ($p=0.0001$), more often female ($p<0.0001$), were more likely to live in the least socioeconomically deprived areas ($p=0.0005$), had better performance status ($p<0.0001$) and lower Charlson comorbidity scores ($p=0.0237$) than those who underwent radical radiotherapy.

To assess the effect of travel time to treatment centre and case-mix on the odds of undergoing curative treatment, univariable and multivariable logistic regression analyses were performed (Table 2). There was a stark drop off in the odds of undergoing surgical resection associated with age over 75 (adjusted OR 0.76, 0.39 and 0.12 for ages 75-79, 80-85 and 85+, respectively, p -trend <0.0001). There was a less pronounced but significant trend of reduced odds of undergoing radical radiotherapy with age with the highest age group (85+) being almost half as likely compared to those aged <55 years of age (adjusted

OR 0.53, 95% CI 0.47-0.61, p-trend <0.0001). Whereas female NSCLC patients were 16% more likely to undergo surgical resection compared to males, there was no association between sex and the odds of undergoing radical radiotherapy. Whereas there was no clear association between diagnosis year and surgical resection in the multivariable model, patients diagnosed more recently were more likely to undergo radical radiotherapy compared to 2009 (adjusted OR 1.41, 95% CI 1.29-1.53 for 2013 versus 2009, p-trend <0.0001). Performance status was more strongly associated with the odds of undergoing surgical resection (adjusted OR 0.02, 95% CI 0.01-0.04 for highest vs lowest, p-trend <0.0001) than radical radiotherapy (adjusted OR 0.04, 95% CI 0.02-0.06 for highest vs lowest, p-trend <0.0001). We observed an increased likelihood of undergoing surgical resection among patients with comorbidity scores 1 and 2 compared with patients without any recorded comorbidity, and patients with comorbidity were also more likely to receive radical radiotherapy. Following multiple imputation, the odds ratio of undergoing surgery remained significant for the group of patients with comorbidity score 2, but no significant trend across comorbidity groups was detected. An attenuated but significant trend remained for radiotherapy. The association of stage with surgical resection reflects a 35% reduced likelihood of patients with stage II disease undergoing surgical resection compared to patients with stage I disease (95% CI 0.61-0.70).

The variation in travel time to nearest surgical treatment centre was greater than that to radiotherapy centre (travel time to thoracic centre: median=30 min, IQR [18-48], travel time to RT centre: median=24 min, IQR [14-35]). Most thoracic surgery units and radiotherapy centres are located in big cities where levels of deprivation tend to be higher. The proportion of patients living in the most deprived areas was highest in the quintile with shortest travel time to a treatment centre (44% for thoracic surgery centres and 37% for radiotherapy centres) and lowest in the furthest quintile (13.8% for thoracic surgery and 17.0% for radiotherapy centres). The odds ratios of undergoing surgical resection decreased with increasing travel time to a thoracic surgery centre (adjusted OR 0.81, 95% CI 0.76-0.87 for travel time >55 min vs ≤15 min) and there was a significant trend in the odds ratios over the five travel time quintiles (p-trend <0.0001). No clear association was observed for radical radiotherapy. Higher levels of socioeconomic deprivation were associated with lower odds of undergoing surgical resection (adjusted OR 0.91, 95% CI 0.85-0.97 for highest vs lowest, p-trend <0.0001), whereas the opposite was observed for radical radiotherapy (adjusted OR 1.16, 95% CI 1.08-1.25 for highest vs lowest, p-trend <0.0001). For receipt of surgical resection, the adverse effect of travel time increased with increasing levels of deprivation, with the highest magnitude of the travel time trend observed for the most deprived group (Table 3a). Patients living furthest away from the nearest thoracic surgery unit and resident in areas with the two highest levels of deprivation had the lowest odds of receiving surgery (adjusted OR 0.72, 95% CI 0.60-0.88 and OR 0.73, 95% CI 0.59-0.91 for deprivation quintiles 4 and 5 respectively). There was no clear pattern of variation in access to radical radiotherapy in relation to travel time and socioeconomic deprivation (Table 3b). For patients resident in the most deprived areas the odds of receiving radical radiotherapy were consistently higher although with little difference by travel time.

Figure 1 shows the significant variation in the use of potentially curative treatment by CCG. The proportion of NSCLC patients receiving curative treatment ranged from 11.8% to 31.7. The proportion undergoing surgical resection ranged from 8.9% to 20.2% (panel a) (England average 13.9%), whereas the proportion receiving radical radiotherapy ranged from 0.4% to 16.4% (panel b) (England average 6.4%). We did not find evidence of either positive or inverse correlation between CCG based rates of surgical resection and rates of radical radiotherapy in the scatterplot (Pearson correlation coefficient $\rho = -0.03$) (panel c). Given the variation in both treatment modalities, we focussed the subsequent survival analyses on CCG variation in intensity of surgical resection and radical radiotherapy separately.

Results from the univariable and multivariable Cox shared-frailty models are shown in Table 4. Compared to patients living in areas with the highest surgical resection rates, higher mortality rates were observed for the lower surgical resection quintiles, and some attenuation was observed when adjusted for case-mix (HR 1.08, 95% CI 1.04-1.12 for lowest vs. highest resection quintile, p-trend 0.0001). A similar magnitude was observed for radical radiotherapy quintile (HR 1.06, 95% CI 1.02-1.10 for lowest vs. highest resection quintile, p-trend 0.0034). Among the treated patients only, the associations were reversed although not statistically significant, and trends not clear.

A sensitivity analysis was performed by repeating logistic and Cox regression analyses with imputed data. With the exception of comorbidity (discussed above) the relationships between the independent variables and treatment, and between treatment intensity and mortality were not materially affected by the imputation performed (supplementary data).

4 Discussion

This study found wide geographical variation in access to potentially curative treatments of 12 to 32% of NSCLC patients receiving potentially curative treatment by CCG, and that this variation stemmed from variation in both surgical resection and radical radiotherapy rates that did not appear to be correlated. The variation in access to both treatment modalities affected survival of NSCLC patients in England. The surgical resection rate of 16% during the study period is in line with previously published results from the National Lung Cancer Audit [20]. Between 2004 and 2008 major surgical resection rates of 17.5-24% are reported in European studies [6, 7, 21]. Rates in England do not compare favourably, and despite improvements toward the end of the study period, overall resection rates remain low by international comparison. There is limited information regarding rates of radical radiotherapy internationally.

In agreement with previously reported studies [22, 23] we found that increasing travel time to treating centre is significantly associated with lower rates of surgical treatment for lung cancer, but the association with radical radiotherapy treatment was less clear. Furthermore, we found that travel time to the nearest thoracic surgery unit exacerbated the effects of socioeconomic deprivation, with the patients living furthest away from the nearest thoracic surgery unit and resident in areas with the two highest levels of deprivation having significantly lower likelihood of undergoing surgical resection. Travel time did

not appear to alter the effects of socioeconomic deprivation on the likelihood of being treated with radical radiotherapy. Travel times to the nearest thoracic centre were greater than for nearest radiotherapy centre, but even when equivalent travel time intervals were analysed, the difference in association persisted (data not shown). An earlier study showed similar associations of a more pronounced association between travel time to nearest hospital and receipt of surgery than radiotherapy in the north of England [23, 24].

Both patient and organisational reasons could be responsible for this. From a patient perspective, travel implications for radiotherapy could be expected to have a greater impact because of the need for repeated treatments, as opposed to a single hospitalisation for surgery. Travel time can also be a significant burden on carers, and an in-patient stay for surgery may constitute a bigger burden on carers if the distance is greater. Patient travel for treatment is frequently provided free of charge for those undergoing radiotherapy whilst the same is not true for carers travelling to visit hospital. Our finding provides valuable information to commissioners and clinicians about a need for increased vigilance to the risk of reduced access to treatment in the presence of longer travel times, particularly in the presence of socio-economic deprivation [25]. Patient hotels in treatment centres are already recommended and targeting their increased use to this patient group could be considered [26, 27].

From a health care organisational perspective, the distance to thoracic centre may be related to a difference in the likelihood of being considered for surgical resection based on the hospital where the patient was first seen. Evidence from the National Lung Cancer Audit has shown that patients with NSCLC first seen in a thoracic surgical centre are more likely to have surgery [28]. Variation in the use of appropriate staging investigations, local availability of complex techniques (such as SABR) and intra-disciplinary team working may contribute to the observed difference in access to radical radiotherapy. These factors have not been accounted for here, and further work is required to investigate whether, and what institutional differences account for this variation in order to identify possible strategies to improve treatment rates and outcomes.

Our findings with regard to access to potentially curative treatment in relation to other patient demographics and tumour characteristics are in line with previous reports with regard to increasing age, male sex, poor performance status and advanced stage all associated with lower odds of receiving potentially curative treatment. We observed an increase in the likelihood of undergoing potentially curative treatment for patients with any comorbidity compared with those with no recorded comorbidity. It is plausible that some patients with comorbid conditions requiring inpatient care were under closer clinical surveillance or had been in contact with the health care system and therefore their lung cancer was discovered at an early stage, making them more likely to receive curative treatment. However, it is of interest, that the associations were much attenuated when we applied multiple imputation to account for the missing data for stage and performance status, raising the possibility that the association may result from residual confounding.

It is of interest that increasing level of socioeconomic deprivation was associated with higher access to radiotherapy, which is in contrast to a reverse association between socioeconomic deprivation and surgical resection. The higher rates of radical radiotherapy in patients living in the more deprived areas may well simply be the inverse of the surgical findings, with more deprived patients more likely to be offered or choose radical radiotherapy over surgery. As noted above SED also further exacerbated the reduction in access to surgery associated with longer travel times.

The differences in access to treatment have a clear effect on the outcomes for lung cancer patients, both for surgical resection and for radical radiotherapy. Some attenuation by case-mix was found. When the survival analyses were restricted to the treated patients only, among the surgically resected patients we see diminishing returns of increasing resection rates, possibly indicating that the high treatment areas include more complicated patients. Among the patients treated with radical radiotherapy no such effect was found, possibly indicating that the rate of radical radiotherapy reported here is well below its optimal level.

This study is strengthened by assessing rates of treatment across the whole of England acknowledging both surgical and radiotherapy treatments delivered with a view to cure. It does, however, have a number of limitations. The surgical resections identified from the inpatient HES data using the OPCS-4 codes provide a robust measure of surgical treatment intensity in England. The radiotherapy data as available from the RTDS proved more difficult, as only summarised numbers of attendances were available and not fractions, and only 73% of records had a valid dose recorded. Using our algorithm, taking into account time between summarised episodes of radiotherapy attendances, SABR identified by proxy using stage and centre information, the proportion of patients identified as receiving radical radiotherapy increased from 6% to 7.15%. A validation study comparing patients as identified from the RTDS as having undergone radical radiotherapy against trust records from two radiotherapy centres revealed a 95% concordance. Although this shows that we may have missed a small proportion of patients receiving radical radiotherapy, it is unlikely that this is differential misclassification. As such, we feel that both the geographical variation observed and the impact on survival is real.

Another limitation of this study is that we did not have information on use of chemotherapy, and therefore cannot assess the impact in difference between radical radiotherapy alone versus chemoradiotherapy. Depending on whether use of chemoradiotherapy varies in the same way that radical radiotherapy does, we may be underestimating the impact this variation has on survival. Furthermore, data on stage, performance status and morphology was frequently missing and varied between the group of patients receiving treatment and those not receiving treatment. To assess the impact of missing data sensitivity analysis was performed by repeating regression analyses following multiple imputation. With the exception of comorbidity (discussed above) the relationships between the independent variables and the treatment likelihood, and between treatment intensity and mortality were not materially affected by the imputation performed.

Finally, CCGs were used as the geographical unit for comparison. These were created following the Health and Social Care Act in 2012, and replaced Primary Care Trusts (PCTs) on 1 April 2013, and as such were not present for the time period covered by the data presented here. We are therefore limited to interpret our findings in terms of geographically based treatment intensity quintiles rather than in terms of commissioning structures. Moreover, potentially curative lung cancer treatments are delivered in tertiary referral centres with patients diagnosed in most hospitals in England. Many of these have MDTs and these should all have surgical and clinical oncology representation (in line with National Institute for Health and Care Excellence Clinical Guidelines) [29]. Ideally case-mix adjusted rates of potentially curative treatment, with appropriate comparisons, would be delivered at MDT level in order to guide service improvement where necessary. The data used in this study do not directly support the necessary analysis due to the complex referral pathways involved and one to many relationship between CCGs and MDTs.

This study demonstrates significant geographical variation in the use of potentially curative treatment for NSCLC, and that there is no correlation between surgical resection and radical radiotherapy rates. In addition, we found that increasing both surgical resection and radical radiotherapy rates are associated with lower population mortality among all NSCLC patients. Whilst influenced by case-mix this association persists after adjustment, suggesting it may be driven by other factors not studied here, for example institutional and environmental factors or unmeasured confounding variables at patient level. Exploring these additional factors will play an important part in understanding the observed variation in curative treatment rates for NSCLC patients across the English NHS and delivering improvements in both access and outcomes.

Acknowledgments

Data for this study was based on patient-level information collected by the National Health Service, as part of the care and support of cancer patients. The data is collated, maintained and quality assured by the National Cancer Registration and Analysis Service, which is part of Public Health England.

The travel times were estimated by Dr Peninah Murage, University of East Anglia, as part of her PhD research on geographical variation in access to cancer services and outcomes.

Ethics

The National Cancer Registration and Analysis Service has approval from the Confidentiality Advisory Group of the National Health Service Health Research Authority to carry out surveillance using the data they collect on all cancer patients under section 251 of the NHS Act 2006. Therefore separate ethical approval was not required for this study.

References

1. Walters, S., et al., *Is England closing the international gap in cancer survival?* Br J Cancer, 2015. **113**(5): p. 848-60.
2. Coleman, M.P., et al., *Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995-2007 (the International Cancer Benchmarking Partnership): an analysis of population-based cancer registry data.* Lancet, 2011. **377**(9760): p. 127-38.
3. Walters, S., et al., *Lung cancer survival and stage at diagnosis in Australia, Canada, Denmark, Norway, Sweden and the UK: a population-based study, 2004-2007.* Thorax, 2013. **68**(6): p. 551-64.
4. Riaz, S.P., et al., *Trends in incidence of small cell lung cancer and all lung cancer.* Lung Cancer, 2012. **75**(3): p. 280-4.
5. Riaz, S.P., et al., *Variation in surgical resection for lung cancer in relation to survival: population-based study in England 2004-2006.* Eur J Cancer, 2012. **48**(1): p. 54-60.
6. Myrdal, G., et al., *Regional differences in treatment and outcome in non-small cell lung cancer: a population-based study (Sweden).* Lung Cancer, 2009. **63**(1): p. 16-22.
7. Wouters, M.W., et al., *Variation in treatment and outcome in patients with non-small cell lung cancer by region, hospital type and volume in the Netherlands.* Eur J Surg Oncol, 2010. **36 Suppl 1**: p. S83-92.
8. Janssen-Heijnen, M.L., et al., *Prevalence of co-morbidity in lung cancer patients and its relationship with treatment: a population-based study.* Lung Cancer, 1998. **21**(2): p. 105-13.
9. Peake, M.D., et al., *Ageism in the management of lung cancer.* Age Ageing, 2003. **32**(2): p. 171-7.
10. Tyldesley, S., et al., *Association between age and the utilization of radiotherapy in Ontario.* Int J Radiat Oncol Biol Phys, 2000. **47**(2): p. 469-80.
11. Morris, E.J., et al., *Wide Variation in the Use of Radiotherapy in the Management of Surgically Treated Rectal Cancer Across the English National Health Service.* Clin Oncol (R Coll Radiol), 2016. **28**(8): p. 522-31.
12. Donaldson, J.W., et al., *Measuring variation in decision making within lung cancer multidisciplinary team (MDT) meetings—a pilot study.* Thorax, 2011. **66**(Suppl 4): p. P153.
13. *The English Indices of Deprivation 2015*, D.f.C.a.L. Government, Editor. 2015.
14. *National Lung Cancer Audit (LUCADA 2013).* <https://digital.nhs.uk/data-and-information/publications/statistical/national-lung-cancer-audit>.
15. *Hospital Episode Statistics (HES 2015)* <https://digital.nhs.uk/data-and-information/data-tools-and-services/data-services/hospital-episode-statistics>.
16. Quan, H., et al., *Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries.* Am J Epidemiol, 2011. **173**(6): p. 676-82.

17. *OPCS Classification of Interventions and Procedures*. 2017; Available from: https://www.datadictionary.nhs.uk/web_site_content/supporting_information/clinical_coding/opcs_classification_of_interventions_and_procedures.asp?shownav=1.
18. Riaz, S.P., et al., *Recent trends in resection rates among non-small cell lung cancer patients in England*. Thorax, 2012. **67**(9): p. 811-4.
19. Bateman, I., et al., in *UK National Ecosystem Assessment Technical Report*. 2011. p. 1067–1152.
20. Beckett, P., et al., *Exploring variations in lung cancer care across the UK--the 'story so far' for the National Lung Cancer Audit*. Clin Med (Lond), 2012. **12**(1): p. 14-8.
21. Imperatori, A., et al., *Resection rate of lung cancer in Teesside (UK) and Varese (Italy): a comparison after implementation of the National Cancer Plan*. Thorax, 2016. **71**(3): p. 230-7.
22. Kelly, C., et al., *Are differences in travel time or distance to healthcare for adults in global north countries associated with an impact on health outcomes? A systematic review*. BMJ Open, 2016. **6**(11): p. e013059.
23. Crawford, S.M., et al., *Social and geographical factors affecting access to treatment of lung cancer*. Br J Cancer, 2009. **101**(6): p. 897-901.
24. Jones, A.P., et al., *Travel time to hospital and treatment for breast, colon, rectum, lung, ovary and prostate cancer*. Eur J Cancer, 2008. **44**(7): p. 992-9.
25. Peake, M.D., *Deprivation, distance and death in lung cancer*. Thorax, 2015. **70**(2): p. 108-9.
26. Department of Health, *Improving Outcomes: A Strategy for Cancer*. 2011.
27. Department of Health Cancer Policy Team, *Radiotherapy in England 2012*. 2012.
28. Rich, A.L., et al., *Inequalities in outcomes for non-small cell lung cancer: the influence of clinical characteristics and features of the local lung cancer service*. Thorax, 2011.
29. *National Institute for Health and Care Excellence Clinical Guidelines [CG121] Lung cancer: diagnosis and management*; . 2011.

Table 1 Patient and tumour characteristics by curative treatment type (surgical resection, radical radiotherapy, and no treatment)

	Total		Surgical treatment		Radical RT treatment		No treatment		Mantel-Haenszel χ^2 (1) df, p-value
	n	col %	n	col %	n	col %	n	col %	
	144,357		20,208	14.0	9,512	6.6	114,637	79.4	
Age									
median	73		69		71		74		5373.362
IQR	[65 80]		[62 75]		[64 77]		[66 82]		0.0001*
Sex									
Male	79,924	55.4	10,514	52.0	5,578	58.6	63,832	55.7	59.5366
Female	64,433	44.6	9,694	48.0	3,934	41.4	50,805	44.3	<.0001
Diagnosis year									
2009	21,935	15.2	2,675	13.2	1,202	12.6	18,058	15.8	305.9995 <.0001
2010	29,743	20.6	3,801	18.8	1,753	18.4	24,189	21.1	
2011	30,504	21.1	4,193	20.8	1,929	20.3	24,382	21.3	
2012	31,389	21.7	4,781	23.7	2,239	23.5	24,369	21.3	
2013	30,786	21.3	4,758	23.6	2,389	25.1	23,639	20.6	
Socioeconomic deprivation quintile									
1 (most affluent)	20,201	14.0	3,077	15.2	1,213	12.8	15,911	13.9	12.2393 0.0005
2	25,986	18.0	3,858	19.1	1,553	16.3	20,575	18.0	
3	28,810	20.0	3,921	19.4	1,831	19.3	23,058	20.1	
4	31,822	22.0	4,222	20.9	2,091	22.0	25,509	22.3	
5 (most deprived)	37,538	26.0	5,130	25.4	2,824	29.7	29,584	25.8	
Performance status score									
0	19,946	13.8	7,294	36.1	2,296	24.1	10,356	9.0	779.136 <.0001
1	32,788	22.7	6,221	30.8	3,782	39.8	22,785	19.9	
2	20,188	14.0	997	4.9	1,544	16.2	17,647	15.4	
3	19,091	13.2	126	0.6	328	3.5	18,637	16.3	
4	6,592	4.6	12	0.1	16	0.2	6,564	5.7	
Not known	45,752	31.7	5,558	27.5	1,546	16.3	38,648	33.7	
Comorbidity score									
0	105,632	73.2	14,852	73.5	6,809	71.6	83,971	73.3	5.1198 0.0237
1	19,941	13.8	2,791	13.8	1,436	15.1	15,714	13.7	
2	10,396	7.2	1,619	8.0	706	7.4	8,071	7.0	
3+	8,388	5.8	946	4.7	561	5.9	6,881	6.0	

Stage									
I	13,963	9.7	7,676	38.0	1,857	19.5	4,430	3.9	449.9742 <.0001
II	7,848	5.4	3,692	18.3	970	10.2	3,186	2.8	
III	20,810	14.4	2,134	10.6	3,342	35.1	15,334	13.4	
IV	53,363	37.0	759	3.8	723	7.6	51,881	45.3	
Not known	48,373	33.5	5,947	29.4	2,620	27.5	39,806	34.7	
Topography									
Trachea	139	0.1	18	0.1	30	0.3	91	0.1	4201.8295 <.0001
Main bronchus	6,919	4.8	222	1.1	449	4.7	6,248	5.5	
Upper lobe	61,035	42.3	11,389	56.4	5,383	56.6	44,263	38.6	
Middle lobe	4,826	3.3	955	4.7	323	3.4	3,548	3.1	
Lower lobe	32,327	22.4	6,506	32.2	2,002	21.1	23,819	20.8	
Overlapping lesion	637	0.4	196	1.0	22	0.2	419	0.4	
Not specified	38,474	26.7	922	4.6	1,303	13.7	36,249	31.6	
Morphology									
Adenocarcinoma	43,340	30.0	10,172	50.3	2,398	25.2	30,770	26.8	6107.4635 <.0001
Carcinoid	3,000	2.1	1,407	7.0	80	0.8	1,513	1.3	
Large cell	1,388	1.0	373	1.9	75	0.8	940	0.8	
Non small cell	19,197	13.3	714	3.5	1,451	15.3	17,032	14.9	
Other specified	336	0.2	136	0.7	9	0.1	191	0.2	
Squamous	32,222	22.3	6,908	34.2	4,161	43.7	21,153	18.5	
Unspecified	44,874	31.1	498	2.5	1,338	14.1	43,038	37.5	

* Kruskal-Wallis equality-of-populations rank test

Table 2 Odds ratios (95% CI) of receiving treatment from univariable and multivariable logistic regression models by (a) surgical resection and (b) radical radiotherapy, including travel time and case-mix.

a)	Total number of patients	Patients undergoing surgical resection		Model 1: unadjusted			Model 2: multivariable*		
	N	N	row %	OR	95% CI		OR	95% CI	
Travel time to thoracic centre									
<=15min	29,370	4,376	14.9	1			1		
15-25min	29,375	4,299	14.6	0.98	0.94	1.02	1.06	1.00	1.14
25-35min	25,023	3,547	14.2	0.94	0.90	0.99	0.97	0.90	1.03
35-55 min	32,900	4,422	13.4	0.89	0.85	0.93	0.88	0.82	0.93
>55 min	26,939	3,486	12.9	0.85	0.81	0.89	0.81	0.76	0.87
NK	750	78	10.4	0.66	0.52	0.84	0.67	0.49	0.91
χ^2						62.29			60.85
p-trend						0.0000			0.0000
Age									
<55 years	8,650	1,816	21.0	1			1		
55-59 years	8,874	1,674	18.9	0.87	0.81	0.94	0.96	0.87	1.06
60-64 years	15,767	3,105	19.7	0.92	0.86	0.98	1.01	0.92	1.10
65-69 years	21,643	4,227	19.5	0.91	0.86	0.97	1.03	0.94	1.12
70-74 years	24,279	4,201	17.3	0.79	0.74	0.84	0.94	0.87	1.03
75-79 years	24,608	3,396	13.8	0.60	0.57	0.64	0.76	0.70	0.83
80-84 years	21,582	1,479	6.9	0.28	0.26	0.30	0.39	0.36	0.44
85+ years	18,954	310	1.6	0.06	0.06	0.07	0.12	0.11	0.14
χ^2						3894.79			862.20
p-trend						0.0000			0.0000
Sex									
Male	79,924	10,514	13.2	1			1		
Female	64,433	9,694	15.0	1.17	1.13	1.20	1.16	1.11	1.21
χ^2						105.72			46.42
p-hetrogeneity						0.0000			0.0000

Diagnosis year									
2009	21,935	2,675	12.2	1			1		
2010	29,743	3,801	12.8	1.05	1.00	1.11	1.07	1.00	1.15
2011	30,504	4,193	13.7	1.15	1.09	1.21	1.04	0.97	1.11
2012	31,389	4,781	15.2	1.29	1.23	1.36	1.04	0.96	1.12
2013	30,786	4,758	15.5	1.32	1.25	1.38	1.01	0.94	1.09
χ^2						182.83			0.09
p-trend						0.0000			0.7613
Socioeconomic deprivation quintile									
1 (most affluent)	20,201	3,077	15.2	1			1		
2	25,986	3,858	14.8	0.97	0.92	1.02	1.00	0.93	1.08
3	28,810	3,921	13.6	0.88	0.83	0.92	0.91	0.85	0.98
4	31,822	4,222	13.3	0.85	0.81	0.90	0.87	0.81	0.93
5 (most deprived)	37,538	5,130	13.7	0.88	0.84	0.92	0.91	0.85	0.97
χ^2						43.16			17.40
p-trend						0.0000			0.0000
Performance status score									
0	19,946	7,294	36.6	1			1		
1	32,788	6,221	19.0	0.41	0.39	0.42	0.45	0.43	0.48
2	20,188	997	4.9	0.09	0.08	0.10	0.13	0.12	0.14
3	19,091	126	0.7	0.01	0.01	0.01	0.03	0.03	0.04
4	6,592	12	0.2	0.00	0.00	0.01	0.02	0.01	0.04
Not known	45,752	5,558	12.1	0.24	0.23	0.25	0.50	0.47	0.53
χ^2						9581.43			3442.79
p-trend						0.0000			0.0000
Comorbidity score									
0	105,632	14,852	14.1	1			1		
1	19,941	2,791	14.0	0.99	0.95	1.04	1.08	1.02	1.15
2	10,396	1,619	15.6	1.13	1.07	1.19	1.30	1.20	1.41
3+	8,388	946	11.3	0.78	0.72	0.83	1.04	0.94	1.15
χ^2						9.93			20.28

p-trend						0.0016			0.0000
Stage									
I	13,963	7,676	55.0	1			1		
II	7,848	3,692	47.0	0.73	0.69	0.77	0.65	0.61	0.70
III	20,810	2,134	10.3	0.09	0.09	0.10	0.06	0.06	0.06
IV	53,363	759	1.4	0.01	0.01	0.01	0.01	0.01	0.01
Not known	48,373	5,947	12.3	0.11	0.11	0.12	0.13	0.12	0.14
χ^2						19405.31			12971.79
p-trend						0.0000			0.0000
Topography									
C33	139	18	12.9	0.65	0.40	1.06	0.36	0.21	0.60
C340	6,919	222	3.2	0.14	0.13	0.17	0.21	0.18	0.25
C341	61,035	11,389	18.7	1			1		
C342	4,826	955	19.8	1.08	1.00	1.16	0.97	0.87	1.07
C343	32,327	6,506	20.1	1.10	1.06	1.14	1.14	1.09	1.19
C348	637	196	30.8	1.94	1.64	2.30	2.38	1.86	3.04
C349	38,474	922	2.4	0.11	0.10	0.11	0.18	0.17	0.20
χ^2						5213.49			2433.29
p-hetogeneity						0.0000			0.0000
Morphology									
Adenocarcinoma	43,340	10,172	23.5	1			1		
Carcinoid	3,000	1,407	46.9	2.88	2.67	3.10	2.15	1.93	2.40
Large cell	1,388	373	26.9	1.20	1.06	1.35	1.12	0.95	1.33
Non small cell	19,197	714	3.7	0.13	0.12	0.14	0.14	0.12	0.15
Other specified	336	136	40.5	2.22	1.78	2.76	2.14	1.65	2.79
Squamous	32,222	6,908	21.4	0.89	0.86	0.92	0.70	0.67	0.73
Unspecified	44,874	498	1.1	0.04	0.03	0.04	0.05	0.04	0.05
χ^2						8809.80			5455.07
p-hetogeneity						0.0000			0.0000

* adjusted for: travel time to nearest thoracic centre, age, sex, diagnosis year, socioeconomic deprivation, performance status, comorbidity score, stage, topography and morphology

b)	Total number of patients	Patients undergoing radical radiotherapy		Model 1: unadjusted			Model 2: multivariable*		
	N	N	row %	OR	95% CI		OR	95% CI	
Travel time to radiotherapy centre									
<=10min	21,043	1,458	5.0	1			1		
10-20min	33,682	2,270	7.7	0.97	0.91	1.04	0.99	0.92	1.06
20-30min	36,724	2,381	9.5	0.93	0.87	1.00	0.97	0.90	1.04
30-40min	26,855	1,806	5.5	0.97	0.90	1.04	1.01	0.93	1.09
>40min	25,303	1,546	5.7	0.87	0.81	0.94	0.91	0.84	0.99
NK	750	51	6.8	0.98	0.73	1.31	0.97	0.72	1.32
χ^2						10.55			3.61
p-trend						0.0012			0.0574
Age									
<55 years	8,650	651	7.5	1			1		
55-59 years	8,874	717	8.1	1.08	0.97	1.21	0.94	0.84	1.06
60-64 years	15,767	1,260	8.0	1.07	0.97	1.18	0.91	0.82	1.01
65-69 years	21,643	1,695	7.8	1.04	0.95	1.15	0.88	0.79	0.97
70-74 years	24,279	1,805	7.4	0.99	0.90	1.08	0.84	0.76	0.93
75-79 years	24,608	1,644	6.7	0.88	0.80	0.97	0.82	0.74	0.91
80-84 years	21,582	1,188	5.5	0.72	0.65	0.79	0.79	0.71	0.88
85+ years	18,954	552	2.9	0.37	0.33	0.41	0.53	0.47	0.61
χ^2						434.84			86.40
p-trend						0.0000			0.0000
Sex									
Male	79,924	5,578	7.0	1			1		
Female	64,433	3,934	6.1	0.87	0.83	0.90	0.97	0.92	1.01
χ^2						44.17			2.12
p-hetrogeneity						0.0000			0.1450
Diagnosis year									

2009	21,935	1,202	5.5	1			1		
2010	29,743	1,753	5.9	1.08	1.00	1.17	1.14	1.05	1.23
2011	30,504	1,929	6.3	1.16	1.08	1.25	1.19	1.10	1.29
2012	31,389	2,239	7.1	1.32	1.23	1.42	1.28	1.18	1.40
2013	30,786	2,389	7.8	1.45	1.35	1.56	1.41	1.29	1.53
χ^2						151.02			68.40
p-trend						0.0000			0.0000
Socioeconomic deprivation quintile									
1 (most affluent)	20,201	1,213	6.0	1			1		
2	25,986	1,553	6.0	0.99	0.92	1.08	0.96	0.88	1.04
3	28,810	1,831	6.4	1.06	0.99	1.15	1.02	0.94	1.11
4	31,822	2,091	6.6	1.10	1.02	1.18	1.02	0.95	1.10
5 (most deprived)	37,538	2,824	7.5	1.27	1.19	1.37	1.16	1.08	1.25
χ^2						69.57			26.02
p-trend						0.0000			0.0000
Performance status score									
0	19,946	2,296	11.5	1			1		
1	32,788	3,782	11.5	1.00	0.95	1.06	1.11	1.05	1.18
2	20,188	1,544	7.6	0.64	0.59	0.68	0.84	0.78	0.90
3	19,091	328	1.7	0.13	0.12	0.15	0.22	0.19	0.25
4	6,592	16	0.2	0.02	0.01	0.03	0.04	0.02	0.06
Not known	45,752	1,546	3.4	0.27	0.25	0.29	0.40	0.37	0.43
χ^2						2022.59			883.63
p-trend						0.0000			0.0000
Comorbidity score									
0	105,632	6,809	6.4	1			1		
1	19,941	1,436	7.2	1.13	1.06	1.19	1.17	1.10	1.24
2	10,396	706	6.8	1.06	0.98	1.15	1.12	1.03	1.22
3+	8,388	561	6.7	1.04	0.95	1.14	1.25	1.14	1.38
χ^2						5.42			34.59
p-trend						0.0199			0.0000

Stage									
I	13,963	1,857	13.3	1			1		
II	7,848	970	12.4	0.92	0.85	1.00	0.81	0.75	0.89
III	20,810	3,342	16.1	1.25	1.17	1.33	1.14	1.07	1.21
IV	53,363	723	1.4	0.09	0.08	0.10	0.11	0.10	0.12
Not known	48,373	2,620	5.4	0.37	0.35	0.40	0.59	0.55	0.63
χ^2						3206.31			2122.87
p-trend						0.0000			0.0000
Topography									
C33	139	30	21.6	2.85	1.90	4.27	3.05	1.99	4.67
C340	6,919	449	6.5	0.72	0.65	0.79	0.85	0.76	0.95
C341	61,035	5,383	8.8	0			1		
C342	4,826	323	6.7	0.74	0.66	0.83	0.81	0.72	0.91
C343	32,327	2,002	6.2	0.68	0.65	0.72	0.70	0.66	0.74
C348	637	22	3.5	0.37	0.24	0.57	0.36	0.23	0.56
C349	38,474	1,303	3.4	0.36	0.34	0.39	0.66	0.62	0.71
χ^2						1130.95			303.89
p-hetogeneity						0.0000			0.0000
Morphology									
Adenocarcinoma	43,340	2,398	5.5	0			1		
Carcinoid	3,000	80	2.7	0.47	0.37	0.59	0.41	0.33	0.52
Large cell	1,388	75	5.4	0.98	0.77	1.24	0.84	0.66	1.06
Non small cell	19,197	1,451	7.6	1.40	1.30	1.49	1.77	1.64	1.90
Other specified	336	9	2.7	0.47	0.24	0.91	0.51	0.26	0.99
Squamous	32,222	4,161	12.9	2.53	2.40	2.67	2.01	1.90	2.13
Unspecified	44,874	1,338	3.0	0.52	0.49	0.56	1.02	0.95	1.11
χ^2						2891.68			912.00
p-hetogeneity						0.0000			0.0000

* adjusted for: travel time to nearest radiotherapy centre, age, sex, diagnosis year, socioeconomic deprivation, performance status, comorbidity score, stage, topography and morphology

Table 3 Odds ratios (95% CI) of receiving treatment by quintiles of travel time and socioeconomic deprivation from univariable and multivariable logistic regression models by (a) surgical resection and (b) radical radiotherapy

a)

		Socioeconomic deprivation								
Travel time	1 least deprived		2		3		4		5 most deprived	
<i>Unadjusted model</i>										
Closest	1		1.02	(0.88 - 1.18)	0.86	(0.74 - 0.99)	0.94	(0.82 - 1.08)	0.94	(0.83 - 1.06)
2	1.00	(0.87 - 1.16)	1.02	(0.88 - 1.17)	0.97	(0.85 - 1.11)	0.85	(0.74 - 0.97)	0.86	(0.75 - 0.98)
3	1.04	(0.90 - 1.20)	0.92	(0.80 - 1.06)	0.89	(0.77 - 1.02)	0.82	(0.71 - 0.94)	0.82	(0.72 - 0.94)
4	0.91	(0.80 - 1.05)	0.91	(0.80 - 1.04)	0.79	(0.69 - 0.90)	0.80	(0.69 - 0.91)	0.76	(0.66 - 0.88)
Furthest	0.92	(0.80 - 1.07)	0.88	(0.77 - 1.01)	0.77	(0.68 - 0.89)	0.70	(0.61 - 0.81)	0.72	(0.61 - 0.83)
<i>Fully adjusted model*</i>										
Closest	1		0.99	(0.81 - 1.22)	0.88	(0.72 - 1.07)	1.01	(0.84 - 1.22)	1.06	(0.89 - 1.26)
2	1.05	(0.86 - 1.29)	1.18	(0.97 - 1.44)	1.16	(0.96 - 1.40)	0.98	(0.81 - 1.18)	1.08	(0.90 - 1.30)
3	1.11	(0.91 - 1.35)	1.02	(0.84 - 1.24)	0.99	(0.82 - 1.21)	0.95	(0.78 - 1.15)	0.92	(0.76 - 1.11)
4	0.99	(0.82 - 1.20)	1.01	(0.83 - 1.21)	0.85	(0.70 - 1.03)	0.85	(0.70 - 1.02)	0.80	(0.66 - 0.97)
Furthest	0.95	(0.78 - 1.16)	0.93	(0.77 - 1.12)	0.84	(0.70 - 1.01)	0.72	(0.60 - 0.88)	0.73	(0.59 - 0.91)

b)

		Socioeconomic deprivation								
Travel time	1 least deprived		2		3		4		5 most deprived	
<i>Unadjusted model</i>										
Closest	1		1.28	(1.00 - 1.63)	1.25	(0.99 - 1.57)	1.23	(0.99 - 1.54)	1.50	(1.22 - 1.85)
2	0.97	(0.77 - 1.23)	1.14	(0.92 - 1.42)	1.29	(1.04 - 1.60)	1.28	(1.04 - 1.58)	1.47	(1.20 - 1.79)
3	1.28	(1.03 - 1.59)	1.12	(0.90 - 1.38)	1.12	(0.90 - 1.38)	1.19	(0.96 - 1.46)	1.39	(1.14 - 1.71)
4	1.09	(0.87 - 1.37)	1.14	(0.92 - 1.43)	1.25	(1.00 - 1.55)	1.33	(1.07 - 1.64)	1.52	(1.23 - 1.87)
Furthest	1.19	(0.95 - 1.51)	1.02	(0.82 - 1.27)	1.14	(0.92 - 1.42)	1.20	(0.96 - 1.49)	1.24	(0.99 - 1.56)
<i>Fully adjusted model*</i>										
Closest	1		1.29	(1.00 - 1.66)	1.20	(0.94 - 1.52)	1.12	(0.89 - 1.41)	1.39	(1.12 - 1.73)
2	0.99	(0.78 - 1.26)	1.09	(0.87 - 1.37)	1.27	(1.02 - 1.59)	1.20	(0.97 - 1.50)	1.35	(1.09 - 1.67)
3	1.34	(1.07 - 1.68)	1.08	(0.87 - 1.36)	1.06	(0.85 - 1.33)	1.12	(0.90 - 1.39)	1.29	(1.04 - 1.60)
4	1.07	(0.84 - 1.36)	1.09	(0.86 - 1.37)	1.20	(0.96 - 1.51)	1.24	(0.99 - 1.55)	1.44	(1.15 - 1.79)
Furthest	1.15	(0.90 - 1.46)	0.99	(0.78 - 1.24)	1.11	(0.88 - 1.39)	1.14	(0.91 - 1.42)	1.13	(0.89 - 1.42)

* adjusted for: age, sex, diagnosis year, performance status, comorbidity score, stage, topography and morphology

Table 4 Mortality hazard ratio (95% CI) for surgical resection and radical radiotherapy treatment intensity quintiles among (a) all NSCLC patients and (b) treated patients only

a)	Surgical resection				Radical radiotherapy		
	HR	95% CI			HR	95% CI	
Model 1: adjusted for age and sex							
Q1 - lowest	1.12	1.09	1.15		1.08	1.05	1.12
Q2	1.05	1.02	1.09		1.05	1.01	1.08
Q3	1.04	1.01	1.08		1.06	1.03	1.09
Q4	1.01	0.98	1.04		1.02	0.99	1.05
Q5 - highest	1				1		
χ^2			61.47				27.80
p-trend			0.0000				0.0000
Model 2: fully adjusted*							
Q1 - lowest	1.08	1.04	1.12		1.06	1.02	1.10
Q2	1.02	0.98	1.06		1.08	1.03	1.13
Q3	1.04	1.00	1.08		1.08	1.03	1.12
Q4	0.99	0.95	1.03		1.05	1.00	1.09
Q5 - highest	1				1		
χ^2			16.1				8.57
p-trend			0.0001				0.0034

* age, sex, diagnosis year, socio-economic deprivation, performance status, comorbidity, stage, topography, morphology

b)	Surgical resection				Radical radiotherapy		
	HR	95% CI			HR	95% CI	
Model 1: adjusted for age and sex							
Q1 - lowest	0.93	0.86	1.01		0.95	0.86	1.05
Q2	0.90	0.83	0.98		1.03	0.94	1.13
Q3	0.96	0.89	1.04		0.99	0.91	1.08
Q4	0.92	0.85	0.99		0.95	0.87	1.03
Q5 - highest	1				1		
χ^2			3.50				0.04
p-trend			0.0614				0.8472
Model 2: fully adjusted*							
Q1 - lowest	0.94	0.87	1.02		0.93	0.85	1.03
Q2	0.90	0.84	0.97		1.05	0.96	1.15
Q3	0.97	0.90	1.04		1.00	0.92	1.08
Q4	0.90	0.84	0.97		0.94	0.87	1.02
Q5 - highest	1				1		
χ^2			2.39				0.06
p-trend			0.1223				0.8104

* age, sex, diagnosis year, socio-economic deprivation, performance status, comorbidity, stage, topography, morphology

Figure 1 The proportions of patients treated with a) surgical resection b) radical radiotherapy by CCG as well as c) the scatter plot of the proportion receiving resection by radiotherapy for each CCG

Supplementary Table A: Odds ratios (95% CI) of receiving treatment from multivariable logistic regression models with imputed data by (a) surgical resection and (b) radical radiotherapy

a)	Multivariable model*		
	OR	95% CI	
Travel time to thoracic centre			
<=15min	1		
15-25min	1.04	0.97	1.12
25-35min	0.96	0.89	1.04
35-55 min	0.86	0.80	0.93
>55 min	0.83	0.76	0.89
NK	0.60	0.43	0.85
χ ²	13.66		
p-trend	0.0002		
Age			
<55 years	1		
55-59 years	0.99	0.88	1.12
60-64 years	1.00	0.90	1.12
65-69 years	1.01	0.91	1.12
70-74 years	0.94	0.84	1.04
75-79 years	0.75	0.67	0.83
80-84 years	0.39	0.34	0.43
85+ years	0.13	0.11	0.15
χ ²	673.13		
p-trend	<0.0001		
Sex			
Male	1		
Female	1.08	1.03	1.14
χ ²	10.07		
p-heterogeneity	0.0015		
2009	1		
2010	1.16	1.06	1.28
2011	1.15	1.05	1.26
2012	1.12	1.02	1.22
2013	1.11	1.01	1.21
χ ²	1.23		
p-trend	0.2681		
Socioeconomic deprivation quintile			
1 (most affluent)	1		
2	1.02	0.94	1.11
3	0.92	0.84	1.00
4	0.88	0.81	0.96
5 (most deprived)	0.90	0.83	0.98
χ ²	14.17		
p-trend	0.0002		

b)	Multivariable model*			
	OR	95% CI		
Travel time to radiotherapy centre				
<=10min	1			
10-20min	0.99	0.92		1.06
20-30min	0.97	0.90		1.04
30-40min	1.00	0.93		1.08
>40min	0.91	0.84		0.98
NK	0.98	0.72		1.34
χ^2	0.08			
p-trend	0.7815			
Age				
<55 years	1			
55-59 years	0.97	0.86		1.09
60-64 years	0.92	0.83		1.03
65-69 years	0.88	0.80		0.98
70-74 years	0.86	0.77		0.95
75-79 years	0.83	0.75		0.92
80-84 years	0.81	0.73		0.91
85+ years	0.56	0.49		0.63
χ^2	73.51			
p-trend	<0.0001			
Sex				
Male	1			
Female	0.95	0.91		1.00
χ^2	4.06			
p-heterogeneity	0.0439			
Diagnosis year				
2009	1			
2010	1.15	1.06		1.25
2011	1.22	1.13		1.32
2012	1.32	1.22		1.42
2013	1.45	1.34		1.57
χ^2	104.06			
p-trend	<0.0001			
Socioeconomic deprivation quintile				
1 (most affluent)	1			
2	0.97	0.90		1.06
3	1.05	0.97		1.13
4	1.06	0.98		1.14
5 (most deprived)	1.22	1.13		1.31
χ^2	40.05			
p-trend	<0.0001			

Performance status score				
0	1			
1	0.46	0.43		0.49
2	0.16	0.15		0.18
3	0.07	0.06		0.09
4	0.07	0.04		0.10
χ^2	2238.93			
p-trend	<0.0001			
Comorbidity score				
0	1.00			
1	0.97	0.90		1.04
2	1.11	1.01		1.22
3+	0.95	0.85		1.06
χ^2	0.07			
p-trend	0.7872			
Stage				
I	1			
II	0.52	0.48		0.56
III	0.07	0.06		0.07
IV	0.01	0.01		0.01
χ^2	13250.56			
p-trend	<0.0001			
Topography				
C33	0.20	0.04		1.02
C340	0.25	0.21		0.29
C341	1			
C342	0.94	0.83		1.06
C343	1.22	1.16		1.29
C348	2.91	2.18		3.87
C349	0.30	0.27		0.33
χ^2	108.64			
p-heterogeneity	<0.0001			
Morphology				
Adenocarcinoma	1			
Carcinoid	1.39	1.21		1.59
Large cell	1.14	0.93		1.39
Non small cell	0.14	0.12		0.15
Other specified	2.88	1.68		4.93
Squamous	0.60	0.56		0.63
Unspecified	0.06	0.05		0.07
χ^2	530.52			
p-heterogeneity	<0.0001			

* adjusted for: travel time to nearest thoracic centre, age, sex, diagnosis year, socioeconomic deprivation, performance status, comorbidity score, stage, topography and morphology

Performance status score				
0	1			
1	1.10	1.04		1.17
2	0.79	0.73		0.85
3	0.24	0.21		0.28
4	0.08	0.06		0.12
χ^2	679.48			
p-trend	<0.0001			
Comorbidity score				
0	1.00			
1	1.12	1.05		1.19
2	1.02	0.94		1.11
3+	1.16	1.05		1.28
χ^2	10.24			
p-trend	0.0014			
Stage				
I	1			
II	0.91	0.83		0.99
III	1.02	0.96		1.09
IV	0.13	0.12		0.15
χ^2	2130.49			
p-trend	<0.0001			
Topography				
C33	2.50	1.15		5.44
C340	0.96	0.86		1.07
C341	1			
C342	0.81	0.71		0.91
C343	0.70	0.66		0.74
C348	0.36	0.23		0.56
C349	0.80	0.75		0.86
χ^2	26.89			
p-heterogeneity	<0.0001			
Morphology				
Adenocarcinoma	1			
Carcinoid	0.32	0.26		0.41
Large cell	0.85	0.67		1.08
Non small cell	1.93	1.80		2.08
Other specified	0.38	0.19		0.74
Squamous	2.05	1.94		2.17
Unspecified	1.13	1.04		1.22
χ^2	163.7			
p-heterogeneity	<0.0001			

* adjusted for: travel time to nearest radiotherapy centre, age, sex, diagnosis year, socioeconomic deprivation, performance status, comorbidity score, stage, topography and morphology

Supplementary Table B Mortality hazard ratio (95% CI) for surgical resection and radical radiotherapy treatment intensity quintiles from multivariable Cox models with imputed data among (a) all NSCLC patients and (b) treated patients only

a)	Surgical resection			Radical radiotherapy		
	HR	95% CI		HR	95% CI	
Model 1: adjusted for age and sex						
Q1 - lowest	1.12	1.10	1.13	1.08	1.06	1.10
Q2	1.06	1.04	1.08	1.04	1.02	1.06
Q3	1.04	1.02	1.06	1.06	1.05	1.08
Q4	1.02	1.00	1.04	1.02	1.00	1.04
Q5 - highest	1			1		
χ^2	172.43			80.74		
p-trend	<0.0001			<0.0001		
Model 2: fully adjusted*						
Q1 - lowest	1.07	1.04	1.09	1.03	1.01	1.05
Q2	1.02	1.00	1.04	1.05	1.04	1.07
Q3	1.04	1.02	1.06	1.05	1.03	1.07
Q4	1.00	0.98	1.02	1.01	0.99	1.02
Q5 - highest	1			1		
χ^2	46.47			26.53		
p-trend	<0.0001			<0.0001		

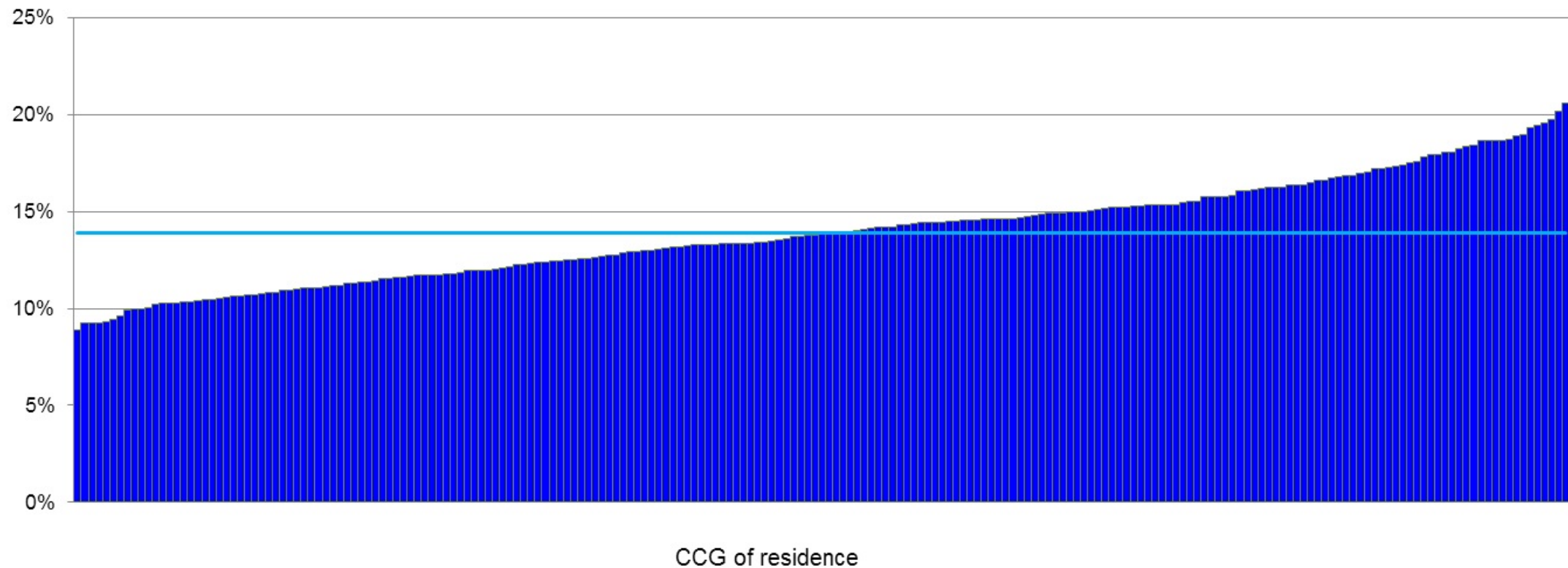
b)	Surgical resection			Radical radiotherapy		
	HR	95% CI		HR	95% CI	
Model 1: adjusted for age and sex						
Q1 - lowest	0.94	0.88	1.00	0.94	0.87	1.02
Q2	0.90	0.85	0.96	1.02	0.95	1.10
Q3	0.94	0.89	1.00	0.98	0.92	1.04
Q4	0.92	0.87	0.98	0.95	0.89	1.01
Q5 - highest	1			1		
χ^2	6.13			0.40		
p-trend	0.0133			0.5265		
Model 2: fully adjusted*						
Q1 - lowest	0.94	0.88	1.01	0.93	0.85	1.01
Q2	0.91	0.85	0.97	1.05	0.98	1.13
Q3	0.96	0.90	1.02	0.99	0.93	1.06
Q4	0.90	0.85	0.95	0.94	0.89	1.00
Q5 - highest	1			1		
χ^2	3.03			0.13		
p-trend	0.0817			0.7232		

* age, sex, diagnosis year, socio-economic deprivation, performance status, comorbidity, stage, topography, morphology

* age, sex, diagnosis year, socio-economic deprivation, performance status, comorbidity, stage, topography, morphology

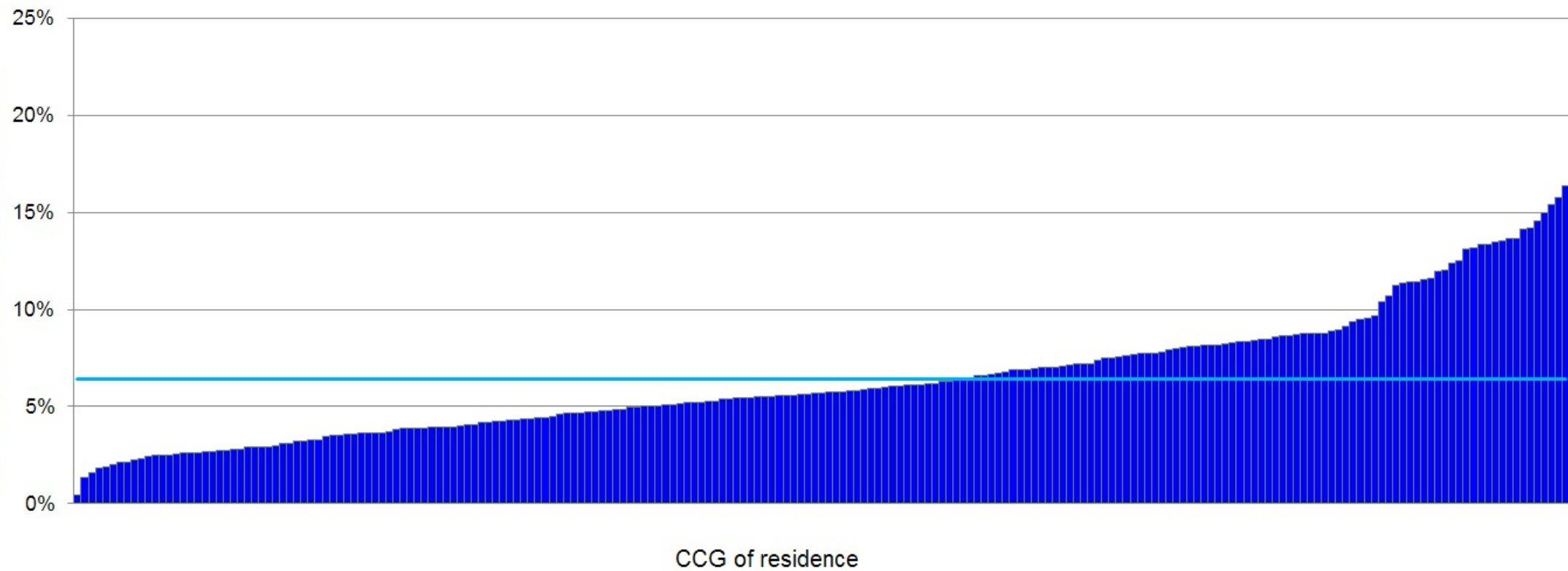
a)

% patients undergoing resection



b)

% patients receiving radical radiotherapy



c)

